REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative, as noted below.

Status of the Claims

Pending claims

Claims 1, 2, 4 to 9, and 14 to 52 are pending.

Claims canceled, added and amended in the instant amendment

Claims 53 and 55 are added. Thus, after entry of the instant amendment, claims 1, 2, 4 to 9, and 14 to 55 will be pending and under consideration.

Outstanding Rejections

Claims 19, 35 and 44 to 52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement – as a "new matter" rejection (page 3 of the instant office action ("OA")). Claims 44, 46, 47, 48 and 49 to 52 stand rejected under 35 U.S.C. §112, second paragraph (pages 3 to 6 of the OA). Claims 1, 2, 4 to 9, 14 to 19, 21, 22, 24 to 30, 32 to 35 and 38 to 52, are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement (pages 6 to 9 of the OA). Claims 27 to 30 (pages 9 to 11 of the OA), claim 31 (pages 11 to 12 of the OA), and claims 40 to 43 (page 12 of the OA), are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Claims 1, 2, 4 to 9 and 14 to 52 are rejected under 35 USC §102(e) as allegedly anticipated by Bylina ("Bylina(a)") U.S. Patent No. 6,368,844, issued, filed August 13, 1998, or, Bylina, et al. ("Bylina(b)") U.S. Patent Application Serial No. (USSN) 2002/0155550, filed April 9, 2002 (page 13 of the OA), or, Short USSN 2003/0078397A1, filed March 06, 2002.

Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the claim amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for isolated or recombinant polypeptides having carboxymethylcellulose activity can be found, inter alia, on page 3, first paragraph, of WO 97/44361 (the publication of PCT/US97/08793).

Drawings

The Patent Office notes that while the "Brief Description of the Drawings" depicts the figures as "Fig 1A to 1X", no such description is found in the figures. It is also noted that the sequences in the Figures lack SEQ ID NOs. The instant amendment to the specification, and the replacement drawings, address this issue.

Sequence compliance

The Patent Office notes that Applicant is required to insert sequence identification numbers of all sequences recited within the claims and/or specification. The instant amendment to the specification, and the replacement drawings, address this issue.

Issues under 35 U.S.C. §112, first paragraph, written description requirement

New matter

Claims 19, 35 and 44 to 52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement – as allegedly containing subject matter not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention – this is a new matter rejection.

In particular, the Patent Office is concerned about support in the specification for polynucleotides or polypeptides having 97% sequence identity to an exemplary sequence, as in

claims 19 and 35. Support for claims directed to polypeptides or nucleic acids having various sequence identities to exemplary polypeptides or nucleic acids of the invention can be found, inter alia, on page 20, first three paragraphs, and page 22, first paragraph; particularly noting line 6 of the first paragraph of page 20, where it is noted that the term "stringent conditions" means hybridization will occur only if there is, inter alia, at least 97% (sequence) identity between sequences. The instant amendment also addresses this issue.

The Patent Office is concerned about support for the methods of claims 44 to 52 (all added in Applicants amendment of May 10, 2004). Applicants respectfully aver that the specification sets forth an extensive description of the claimed invention. For example, support for claims directed to methods for converting plant biomass into fuels and chemicals (e.g., claim 44) can be found, inter alia, on page 28, lines 16 to 17; see also page 1, lines 17 to 18. Support for claims directed to methods for using a polypeptide of the invention in the detergent and textile industry (e.g., claim 45) can be found, inter alia, on page 28, lines 18 to 19. Support for claims directed to methods for using a polypeptide of the invention for producing a feed, e.g., an animal feed (e.g., claims 46 and 50), can be found, inter alia, on page 28, line 19. Support for claims directed to methods for using a polypeptide of the invention in waste treatment (e.g., claim 47) can be found, inter alia, on page 28, line 19. Support for claims directed to methods for using a polypeptide of the invention in a fruit juice industry or a brewing industry (e.g., claims 48 and 52) can be found, inter alia, on page 28, lines 19 to 20. Support for claims directed to methods for using a polypeptide of the invention in a textile industry (e.g., claim 49) can be found, inter alia, on page 28, lines 18 to 19. Support for claims directed to methods for using a polypeptide of the invention in a detergent (e.g., claim 51) can be found, inter alia, on page 28, lines 18 to 19.

Accordingly, because the claims are sufficiently supported in the specification to satisfy the written description requirement of section 112, first paragraph, the "new matter" rejection under 35 U.S.C. §112, first paragraph, can be properly withdrawn.

Issues under 35 U.S.C. §112, second paragraph

Claims 44, 46, 47, 48 and 49 to 52 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The phrase "fuels and chemicals"

The Patent Office alleges the metes and bounds of the phrase "fuels and chemicals" in claim 44 is not clear, because it allegedly is not clear what types of fuels and chemicals are encompassed by the phrase, and the specification does not have a specific definition of the phrase. After entry of the instant amendment, claim 44 reads on a method for converting plant biomass into fuels and chemicals comprising contacting a plant biomass comprising carboxymethylcellulose with an effective amount of a polypeptide of claim 1, thereby enzymatically converting the plant biomass into a fuel or a chemical. Applicants believe the amendment addresses this issue.

The legal standard for definiteness under section 112, second paragraph, is whether a claim reasonably apprises those of skill in the art of its scope. In re Warmerdam, 33 F.3d 1354,31 USPQ2d 1754, 1759 (citing Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d at 1217, 18 USPQ2d at 1030). If the claims read in light of the specification reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the claims satisfy the requirements of section 112, second paragraph. North American Vaccine Inc. v. American Cyanamid Co., 7 F.3d 1571, 28 USPQ 1333, 1339 (Fed. Cir. 1993) (citing Shatterproof Glass Corp. v. Libbey-Owens Ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir. 1985), cert. dismissed, 474 U.S. 976 (1985). See MPEP 2173.02 and MPEP 2173.05, pages 2100-205, 207, Rev. 2, May 2004.

Applicants respectfully assert that the phrase "fuels and chemicals" in claim 44, read in light of the specification and the prior art, reasonably apprises those skilled in the art both of the utilization and scope of the invention. The "fuels and chemicals" are generated by the enzymatic conversion (using an enzyme of the invention) of carboxymethylcellulose in plant biomass into a fuel or a chemical. The phrase "fuels and chemicals" itself is well known in the art. Accordingly,

the skilled artisan is reasonably apprised of the metes and bounds of the "fuels and chemicals" in claim 44.

The phrase "produces an animal feed"

The Patent Office alleges the metes and bounds of the phrase "produces an animal feed" in claim 46 is not clear, because it allegedly is not clear as to how hydrolysis of CMC cellulose or glycosidic cleavage of a chemical bond produces an animal feed.

As noted above, if the claims read in light of the specification reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the claims satisfy the requirements of section 112, second paragraph. The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. MPEP 2173.02, pg 2100-205, Rev. 2, May 2004.

The specification in the "background" section on pages 1 to 2, describes why hydrolysis of cellulose converts it such that the hydrolysis products of cellulose can be used as a source of stored fuel by animals, see, e.g., the last paragraph page 1, and the first paragraph page 2. Thus, using the teaching of the specification, one skilled in the art would have understood how hydrolysis of CMC cellulose or glycosidic cleavage of a chemical bond in cellulose produces an animal feed, and thus would have understood the phrase "produces an animal feed" with a reasonable degree of clarity and particularity.

The phrase "waste treatment"

The Patent Office alleges the metes and bounds of the phrase "waste treatment" in claim 47 is not clear, because it allegedly is not clear as to what types of wastes are encompasses by the phrase. The instant amendment addresses this issue. After entry of the instant amendment, the polypeptide used in the method of claim 47 is employed in treatment of cellulose-comprising wastes for degrading carboxymethylcellulose or for hydrolyzing a beta 1,4 glycosidic bond in a cellulose.

The phrase "polypeptide further comprises a textile"

The Patent Office alleges the metes and bounds of the phrase "polypeptide further comprises a textile" in claim 49 is not clear, because it allegedly is not clear as to how a polypeptide can further comprise a textile. The instant amendment, as suggested by the Examiner, addresses this issue.

The phrase "polypeptide further comprises a feed"

The Patent Office alleges the metes and bounds of the phrase "polypeptide further comprises a feed" in claim 50 is not clear, because it allegedly is not clear as to how a polypeptide can further comprise a feed. The instant amendment, as suggested by the Examiner, addresses this issue.

The phrase "polypeptide further comprises a detergent"

The Patent Office alleges the metes and bounds of the phrase "polypeptide further comprises a detergent" in claim 51 is not clear, because it allegedly is not clear as to how a polypeptide can further comprise a detergent. The instant amendment, as suggested by the Examiner, addresses this issue.

The phrase "polypeptide further comprises a juice or brew"

The Patent Office alleges the metes and bounds of the phrase "polypeptide further comprises a juice or brew" in claim 51 is not clear, because it allegedly is not clear as to how a polypeptide can further comprise a juice or brew. The instant amendment, as suggested by the Examiner, addresses this issue.

Issues under 35 U.S.C. §112, first paragraph, enablement requirement

Claims 1, 2, 4 to 9, 14 to 19, 21, 22, 24 to 30, 32 to 35 and 38 to 52, are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Patent Office states that the specification is enabling for an endoglucanase of SEQ ID NO:46, a polynucleotide of SEQ ID NO:45 encoding same, and vectors and host cells comprising the polynucleotide.

However, it is alleged that the specification does not provide reasonable enablement for:

- the claimed genus of polynucleotides or polypeptides having 70%, 90%, 95% or 97% sequence identity to an exemplary sequence of the invention; or,

- cellulase polypeptides having 30 or 50 consecutive amino acids of SEQ ID NO:46; or,

- cellulase polypeptides having 30 or 50 consecutive amino acids of the genus encompassing 70%, 90%, 95% or 97% sequence identity to the exemplary SEQ ID NO:46; or,

- probes comprising 15, 25, 35 or 50 nucleotides of polynucleotide having a 70% sequence identity to SEQ ID NO:45.

The Patent Office alleges that because the claimed genera are very large guidance must be provided to determine which changes can be tolerated in a protein's amino acid sequence to obtain a desired activity to practice the invention without undue experimentation.

Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polypeptides having endoglucanase or cellulase activity, and the nucleic acids that encode them, to practice the claimed invention – and will provide evidence and expert declaration to support this argument.

However, Applicants respectfully aver that the Patent Office has not met its initial burden to establish a reasonable basis to question the enablement provided for the claimed invention, and as specifically addressed, below, how the art used to support the Office's enablement rejection is not sufficient to rebut the presumptively enabled specification.

In order to make a rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject

matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). See also MPEP §2164.04, rev. 2, May 2004, pg 2100-189.

The Patent Office cited art to support its *prima facie* case of lack of enablement, where the cited art, Ngo, et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al. (Ed.) ("Ngo"), allegedly supports the unpredictability of the art in predicting function from a polypeptide primary structure. However, this reference is not sufficient to rebut the presumption of enablement. Ngo is not directed to whether, or not, making and screening a large number of nucleic acid and polypeptide variants would have constituted undue experimentation to one skilled in the art at the time of the invention.

Ngo is a review chapter from a 1994 publication that opines that, at least as of 1994, there was no efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. In fact, Ngo's data suggested that most changes in a polypeptide's amino acid sequence (e.g., non-binding or non-catalytic site amino acid residues) are not important in determining, or changing, binding or catalytic specificity. Thus, Ngo actually supports the idea that most changes in a polypeptide's amino acid sequence will result in little or no effect on its specificity or activity, and that one of skill in the art could easily target a minimum number of residues to generate a limited number of enzyme variants to generate desired active (enzyme) variants. Thus, the Patent Office has provided insufficient reasons why one of ordinary skill in the art would not have had a reasonable expectation of success in making and identifying the claimed genus of endoglucanase polypeptides.

The Patent Office also makes the unsupported allegation that it was not routine in the art to screen for multiple substitutions or modifications in a sequence, and the result of such modifications was unpredictable. However, as supported by Dr. Jay Short's declaration (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art for screening enzymes for endoglucanase/ cellulase activity was very high. Dr. Short declares that procedures for making endoglucanase and cellulase enzyme fragments and sequence variations, e.g., with substitutions, deletions, insertions, and additions, were routine in the art at the time of the invention of the above-referenced patent application. He declares that assays for identifying endoglucanase and cellulase enzyme fragments were conventional and routine in the art at the time of the invention. Dr. Short declares that assays for identifying variant polypeptides having endoglucanase and cellulase activity were conventional and routine in the art at the time of the invention. For example, assays for identifying polypeptides having endoglucanase activity are described in the specification, e.g., on page 17, line 6 to page 18, line 7. Dye-based techniques can be used in cup-plate diffusion assays with excellent sensitivity for the determination of endoglucanase activity in culture filtrates or during enzyme purification steps (see first paragraph, page 18), as further noted in Example 1, page 36. Dr. Short declares that endoglucanase activity assays also were well known in the art at the time of the invention, e.g., as described in USPNs 4,081,328; 4,904,599; 5,110,735; 5,366,884, to list only a few examples. Many of these assays could have been adapted and used in high-throughput screening assays, which were well known in the art at the time of the invention. Dr. Short declares that using the teaching of the specification one of ordinary skill in the art would have been able to routinely make and use the claimed genus of nucleic acids and polypeptides without undue experimentation.

Dr. Short also declares that use of high through-put screening assays is an example of the high state of art at the time of the invention for screening polypeptides for endoglucanase and cellulase enzyme activity. For example, at the time of the invention high through-put screening assays, including *in vitro* and *in vivo* (e.g., whole cell) nucleic acid expression and enzyme screening protocols were well known in the art. Dr. Short also declares that the specification sets forth exemplary endoglucanase screening assays to determine if a polypeptide is within the scope of the claimed genus – and these or many of the other well known endoglucanase and cellulase assays

could have been used in high through-put screening assays. Dr. Short also declares that because screening assays known in the art at the time of the invention, including high through-put enzyme screening assays, predictably gave positive results (identifying enzymes with a desired activity) it would not have taken undue experimentation to make the genus of polypeptides of the invention.

Dr. Short also declares that methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. He declares that it would not have been necessary for the skilled artisan to understand which regions of the enzyme could be modified to obtain a desired activity, e.g., to generate a variant a function or activity, or, which regions of the enzyme could be modified without loss of a function or activity. Dr. Short also declares that it would not have been necessary for the skilled artisan to understand which specific regions of enzyme sequence or structure needed to be modified without affecting function or activity to routinely generate the claimed genus of polypeptides. Methods for making and screening sequence modifications and enzyme fragments, including high through-put enzyme screening assays, were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate endoglucanase-encoding sequences without need of knowing which specific regions of a sequence or structure affected function or activity. Dr. Short also declares that the specification provided sufficient guidance to one of ordinary skill in the art to make the genus of polypeptides to practice the invention. Accordingly, Applicants respectfully aver that it would not have been necessary for one skilled in the art to understand which specific regions of enzyme structure could be modified to generate the claimed genus of polypeptides without undue experimentation.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention. Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983). Enablement is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L.

Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Experimentation is not considered undue, even if extensive, if it is routine or if the specification provides reasonable guidance regarding the direction of experimentation -- time and difficulty are not determinative of undue experimentation if the experimentation is routine. See PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996); In re Wands, 858 F.2d at 736-40, 8 USPQ2d at 1403-7; Hybritech, Inc. v. Monoclonal Antibodies, Inc.,802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987) (acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."). Thus, enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit.

Analogously, practitioners of the biological sciences for the instant invention also recognized the need to screen numbers of negatives to find a sample that had the desired properties, e.g., endoglucanase activity. As declared by Dr. Short, the screening procedures used to make and identify nucleic acids and polypeptides of the invention, including high throughput screening assays, were all well known in the art at the time the application was filed. These procedures provided routine protocols for the skilled artisan that yielded predictably positive results – making and identifying endoglucanase enzymes having a desired activity. Furthermore, as noted above, the specification contained sufficient information – a reasonable amount of guidance - regarding making and identifying the claimed genus of polypeptides as to enable one skilled in this art to make and use the claimed invention. Thus, the skilled artisan using Applicants' written disclosure could make the claimed genus of nucleic acids and polypeptides without undue experimentation.

Further addressing the Patent Office's concerns that because the claimed genera are very large sufficient guidance must be provided to determine which changes can be tolerated in a protein's amino acid sequence to obtain a desired activity to practice the invention without undue

experimentation, Applicants respectfully note that if the skilled artisan needed guidance as to which amino acid residues could be modified to obtain structural or functional variants of an enzyme of the invention (Applicants have maintained that it would not have been necessary for one skilled in the art to understand which specific regions of enzyme structure could be modified to generate the claimed genus of polypeptides without undue experimentation), that information was, inter alia, readily available in the form of endoglucanase and cellulase sequences known in the art at the time of the invention. A routine, simple sequence alignment comparison of known endoglucanase and cellulase sequences would have identified regions of identity and dissimilarity to provide guidance to the skilled artisan as to which sequences could be changed, or not changed, to generate structural and/or functional variations of an exemplary endonucleases of the invention. As illustrated in the attached sequence alignment (see Exhibit A) of a random selection of endoglucanases and cellulases known in the art at the time of the invention (e.g., sequences known prior to May 22, 1997; NCBI records for each of these prior art sequences is attached as Exhibit B), including the exemplary SEQ ID NO:45 of the invention, regions of common structural identity between endoglucanases and cellulases were readily identifiable. The sequence alignment highlights in colors regions of structural identity, with yellow representing regions of common structural identity between the endonucleases - there are six completely conserved residues between the compared sequences, highlighted in yellow. Thus, if the skilled artisan desired some guidance as to which amino acid residues could be modified to obtain structural or functional variants of an enzyme of the invention, that information was readily available at the time of the invention.

Further guidance regarding endoglucanase structure and active sites was available if desired to the skilled artisan at the time of the invention, e.g., see Taylor, et all, "Conformational modeling of substrate binding to endocellulase E2 from Thermomonospora fusca," Protein Eng., (1995) Nov 8(11):1145-1152, providing a model structure based on a crystallographically determined structure of an endocellulase; Spezio et al., "Crystal structure of the catalytic domain of a thermophilic endocellulase," Biochemistry, (1993) Sep 28;32(38):9906-16, providing a high-resolution structure of the catalytic domain of the thermophilic endocellulase E2; Sakon, et al., "Crystal structure of thermostable family 5 endocellulase E1 from Acidothermus cellulolyticus in complex with cellotetraose," Biochemistry, 1996 Aug 20;35(33):10648-60, providing a crystal

structure of the catalytic domain of the thermostable endocellulase E1 in complex with a substrate; Warren, et al., "Sequence conservation and region shuffling in an endoglucanase and an exoglucanase from Cellulomonas fimi," Proteins, 1986 Dec;1(4):335-41, discussing conserved active site sequences in endoglucanases; to list only a few examples.

Accordingly, while not necessary, but if desired, one skilled in the art at the time of the invention had many sources of guidance, in addition to the specification, to start from an exemplary nucleic acid or polypeptide of the invention and determine which nucleic acids/ amino acid residues could be modified, substituted, deleted or inserted into a sequence to make, identify, screen for and use structural and/or functional variants of the exemplary and SEQ ID NO:46, without undue experimentation. Thus, if desired, the skilled artisan had sufficient guidance to determine which changes could be tolerated in a protein's amino acid sequence to obtain a desired activity to practice the invention without undue experimentation.

Specifically addressing the allegation that the specification does not enable the skilled artisan to make and use probes comprising 15, 25, 35 or 50 nucleotides of polynucleotide having a 70% sequence identity to SEQ ID NO:45 (see page 7, lines of the OA), Applicants respectfully note that the specification, e.g., on page 8, line 17, to page 9, line 5, and page 20, lines 1 to 11, sufficiently teaches the skilled artisan how to make nucleic acids that hybridize under stringent conditions to exemplary nucleic acids of the invention. Also, as declared by Dr. Short, it was considered routine to design and screen for probes of 15, 25, 35 or 50 nucleotides in length that could hybridize under stringent conditions to a desired polynucleotide.

In light of these remarks and the declaration and evidence provided herein, Applicants respectfully submit that the pending claims are fully enabled by the specification to meet the requirements of 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §112, first paragraph, written description requirement

Claims 27 to 30 (pages 9 to 11 of the OA), claim 31 (pages 11 to 12 of the OA), and claims 40 to 43 (page 12 of the OA), are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

Claims 27 to 30

Claims 27 and 28 are directed to polypeptides having endoglucanase or cellulase activity comprising at least 30 or 50 amino acid residues of a polypeptide having at least 70% sequence identity an amino acid sequence as set forth in SEQ ID NO:46. Claims 29 and 30 are significantly narrower in scope, being directed to polypeptides having endoglucanase or cellulase activity comprising at least 30 or 50 amino acid residues of a polypeptide having an amino acid sequence as set forth in SEQ ID NO:46. It is alleged that these genera are sufficiently large and variable that disclosure of a single specie does not put one of skill in the art in possession of all species within the claimed genus.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., a % sequence identity or stringent hybridization to an exemplary nucleic acid or polypeptide, e.g., SEQ ID NO:45 or SEQ ID NO:46) and function (e.g., encoding a polypeptide having endoglucanase/ cellulase activity) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully aver that the disclosed endoglucanase/ cellulase species of the claimed invention, SEQ ID NO:45 and SEQ ID NO:46, are sufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genera. In fact, both the Patent Office and the Federal Circuit set forth conditions where a single species is sufficient to put one of skill in the art in possession of the attributes and features of all species within a genus, where the genus is defined in terms of shared physical and structural properties with the single species.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph, and note that the guidelines state

that a description of a genus of polynucleotides in terms of its physico-chemical properties, e.g., a % sequence identity, to a single exemplary species, and a common function satisfies the written description requirement of section 112, first paragraph, for the genus of polynucleotides.

In Example 14 of the Guidelines (a copy of which is attached as Exhibit C), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of Example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of claimed nucleic acids and polypeptides are described by structure (the exemplary SEQ ID NO:45 and SEQ ID NO:46), a physico-chemical property (a percent sequence identity to an exemplary sequence or stringent hybridization to an exemplary nucleic acid) and function (having endoglucanase/ cellulase activity). All species of the genus of claimed nucleic acids and polypeptides must have at least 70% or more sequence identity to a sequence as set forth in SEQ ID NO:45 or SEQ ID NO:46. Because the USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, stringent hybridization) and a defined function, the claimed genus of polypeptides and nucleic acids also meet the written description requirements of section 112.

The Federal Circuit has applied the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and

Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The genus of polypeptides used in the claimed methods also fully complies with the requirements for written description of a genus as set forth in University of California v. Eli Lilly & Co.. In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406. The Lilly court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The instant claims clearly set forth specific structural and physical characteristics of the claimed endoglucanases/ cellulases. In one aspect, the genus of nucleic acids and polypeptides all must have endoglucanase/ cellulase activity (or encode the enzyme) and a specific physical characteristic, e.g., a % sequence identity to the exemplary SEQ ID NO:45 or SEQ ID NO:46. Therefore, the genus of claimed endoglucanases/ cellulases is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem. Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613. The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines, note discussion, above). The Guidelines apply to proteins as well as DNAs. The Enzo court also stated:

> Similarly, in this court's most recent pronouncement, it noted:
>
> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the functions of the claimed enzymes are sufficiently correlated to a particular, known structure (the exemplary sequence) and a physical (physico-chemical) property (percent sequence identity or stringent hybridization). Accordingly, the species of claimed polypeptides are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. In re Herschler, 591 F.2d 693, 700, 200 USPQ 711,717 (CCPA 1979). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

Accordingly, Applicants respectfully aver that the exemplary species SEQ ID NO:45 and SEQ ID NO:36 are sufficient to one of skill in the art of a genus of polypeptides having endoglucanase or cellulase activity comprising at least 30 or 50 amino acid residues of a polypeptide having at least 70% sequence identity an amino acid sequence as set forth in SEQ ID NO:46. Applicants also respectfully aver that the exemplary species SEQ ID NO:45 and SEQ ID NO:36 are sufficient to one of skill in the art of a genus of polypeptides having endoglucanase or cellulase activity comprising at least 30 or 50 amino acid residues of a polypeptide having an amino acid sequence as set forth in SEQ ID NO:46. Applicants respectfully submit that the pending claims 27 to 30 meet the written description requirement under 35 U.S.C. §112, first paragraph.

Claim 31

Claim 31 is directed to a genus of polypeptides having endoglucanase or cellulase activity comprising an amino acid sequence as set forth in SEQ ID NO:46 and having at least one conservative amino acid substitution, wherein the conservative amino acid substitution comprises: a replacement, one for another, among the aliphatic amino acids Ala, Val, Leu and Ile; or an interchange of the hydroxyl residues Ser and Thr; or an exchange of the acidic residues Asp and Glu; or a substitution between the amide residues Asn and Gln; or an exchange of the basic residues Lys and Arg; or a replacement among the aromatic residues Phe, Tyr. It is alleged that the written description requirement has not been met because, inter alia, no description of the modified polypeptide sequences encompassed by the claims has been provided.

However, Applicants respectfully aver that they have set forth very specific parameters for defining the claimed genus. For example, only specifically defined conservative amino acid substitutions can be made to the exemplary SEQ ID NO:46, as expressly set forth in the claim (e.g., wherein the conservative amino acid substitution comprises: a replacement, one for another, among the aliphatic amino acids Ala, Val, Leu and Ile, etc). As noted above, the claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. The specific delimited parameters of what conservative amino acid substitutions can be made to an exemplary sequence clearly allow one of ordinary skill in the pertinent art to recognize from the disclosure that Applicants invented the claimed subject matter.

It is also alleged that the genus encompasses a genus having a wide variety of functions. However, only polypeptides having endoglucanase or cellulase activity are within the scope of the claimed invention.

It is also alleged that this genus is sufficiently large and variable that disclosure of a single specie does not put one of skill in the art in possession of all species within the claimed genus. However, Applicants respectfully aver that exemplary species SEQ ID NO:45 and SEQ ID

NO:46 are sufficient to allow one of ordinary skill in the pertinent art to recognize from the disclosure that Applicants invented the claimed subject matter. For reasons analogous to those discussed for claims 27 to 30, above, this genus is described by structure (the exemplary SEQ ID NO:46), a physico-chemical property (the specific delimited parameters of what conservative amino acid substitutions can be made to SEQ ID NO:46) and function (having endoglucanase/ cellulase activity). Because the USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (a conservative amino acid substitution) and a defined function, the genus of claimed polypeptides meet the written description requirements of section 112. Applicants respectfully submit that the pending claim 31 meets the written description requirement under 35 U.S.C. §112, first paragraph.

Claims 40 to 43

Claim 40 to 43 are directed to a genus of probes comprising at least 15, 25, 35 or 50, contiguous nucleotides of a nucleic acid encoding a polypeptide having endoglucanase or cellulase activity and having a nucleic acid sequence having at least 70% sequence identity to a sequence as set forth in SEQ ID NO:45. It is alleged that the specification does not contain any disclosure of all DNA sequences encompassed by the claims.

However, as noted above, the claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. In the discussion addressing claims 27 to 30, above, Applicants discussed above why the claimed genus of nucleic acids encoding a polypeptide having endoglucanase or cellulase activity and having at least 70% sequence identity to a sequence as set forth in SEQ ID NO:45 meets the written description requirement of section 112, first paragraph, i.e., that the application describes the claims such that one having ordinary skill in the pertinent art would recognize from the disclosure that Applicants invented the claimed subject matter.

The additional limitation – that this genus encompasses a genus of probes comprising at least 15, 25, 35 or 50, contiguous nucleotides – is also sufficiently described in the specification such that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. For reasons analogous to those discussed for claims 27 to 30, above, this genus is described by structure (the exemplary SEQ ID NO:46), a physico-chemical property (the specific length of the nucleic acid, and, by percent sequence identity) and function (after entry of the instant amendment, a probe capable of hybridizing to an exemplary sequence). Because the USPTO guidelines recognize that written description is met for a genus of nucleic acids (probes) described by structure, a physico-chemical property and a defined function, the genus of claimed polynucleotides meet the written description requirements of section 112. Applicants respectfully submit that the pending claims 40 to 43 meet the written description requirement under 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Claims 1, 2, 4 to 9 and 14 to 52 are rejected under 35 USC §102(e) as allegedly anticipated by Bylina ("Bylina(a)") U.S. Patent No. 6,368,844, issued, filed August 13, 1998, or, Bylina, et al. ("Bylina(b)") U.S. Patent Application Serial No. (USSN) 20020155550, filed April 9, 2002, or, Short USSN 2003/0078397A1, filed March 06, 2002.

Applicants respectfully note that the instant application is a utility application filed under 35 USC 371, as a national phase of international application PCT/US97/08793, filed May 22, 1997, which has a priority document USSN 08/651,572, filed May 22, 1996. Accordingly, because neither Bylina(a), filed August 13, 1998, Bylina(b), filed April 9, 2002, nor Short USSN 2003/0078397A1, filed March 06, 2002, is prior art to the instant application, Applicants respectfully aver that the rejection of the claims under 35 U.S.C. §102(e) can be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §102(e) and objections to the drawings and specification. In view of the above, claims in this application after entry of the instant amendment are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 564462000502. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 7205133.

Dated: January 19, 2005

Respectfully submitted,

By _____

Gregory P. Einhorn
Registration No.: 38,440
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-5133

Attachments

sd-239947

AMENDMENTS TO THE DRAWINGS

The attached sheets of drawings include changes to Figures 1A to 1X. These sheets replace the original sheets representing Figures 1A to 1X. In the replacement figures, the previously omitted designation (labeling) as Figure 1A - 1 X, and the SEQ ID NO:, as appropriate, have been added.

Attachment: Replacement sheets